

DETAILED ACTION

Response to Amendment

1. Amendment to claims filed 5/24/10 is acknowledged. Currently, claims 18-38 are pending. Claims 1-17 are canceled. Claims 34 and 38 are currently amended. Claims 34 and 38 are withdrawn.
2. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Response to Arguments

3. Applicant's arguments, see applicant's remarks, pages 6-8 , filed 5/24/10, with respect to the rejection(s) of claim(s) 18 under 103(a) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of further secondary reference.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 18-19 and 21-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmermann (US 6465226) in view of Huang et al. (NPL document "Preparation and structure of silicon doped tin oxide composites using an advanced ultrasonic spray method").

Regarding claim 18, Zimmermann teaches a process for preparing microspheres comprising an ionically crosslinked polymer, the process comprising:

(a) producing liquid aerosol droplets from a solution comprising an ionically crosslinkable polyionic polymer into a gas stream comprising compressed air and the droplets by using a nebulizing nozzle;

(b) transferring the gas stream into a gelling solution comprising bivalent or trivalent ions, whereby crosslinked polymer microspheres are formed (abstract, col. 2, lines 65 to col. 3, lines 29, col. 6, lines 38-45, col. 7, lines 28-31).

Zimmermann does not positively characterize the gas stream as continuous. However, it is obvious that the gas stream is continuous since a constant airflow is needed to separate the droplets from the nozzle (abstract, col. 3, lines 8-15).

Zimmermann does not positively characterize a separating step of the microspheres from the gelling solution. However, it is inherent that the microspheres are separated from the gelling solution since Zimmermann teaches a dwell time of 10-15 minutes of the microspheres in the precipitation bath (col. 3, lines 24-29). Zimmermann does not teach using an ultrasonic nebulizer for forming the continuous gas stream.

However, Huang et al. teaches a process for preparation of a homogeneous, ultrafine powder by generating aerosol by an ultrasonic nebulizer. The precursor solution is atomized by

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the ultrasonic nebulizer, carried through the tubing to the nozzle by a carrier gas (air or oxygen) (see pages 205-206). It would have been obvious to one of ordinary skill in the art at the time of the invention to employ the ultrasonic mobilization method disclosed in Huang et al. in Zimmermann since Huang et al. teaches that atomizing a precursor solution by the ultrasonic nebulizer produces homogeneous, ultrafine powders having a particle size of about 100 nm (see pages 205-206).

Regarding claim 19, Zimmermann teaches that the ionically crosslinkable polymer is a polyanionic polymer and the gelling solution comprises a polyvalent cation (abstract, col. 4, lines 18-19, col. 6, lines 9-22 and 43-45).

Regarding claim 21, Zimmermann teaches that the ionically crosslinkable polymer is a polyanionic polymer and the gelling solution comprises di-, multi- or polyvalent cations (col. 4, lines 18-19 and col. 6, lines 38-45).

Regarding claims 22-24, Zimmermann teaches that the polyanionic polymer is alginate (abstract, col. 6, lines 9-21 and col. 7, lines 28-31), which is a salt of alginic acid.

Regarding claim 25, Zimmermann teaches that in step (a), the polyanionic polymer is present in a concentration of less than 5% by weight (col. 2, lines 56-63).

Regarding claims 26-27, Zimmermann teaches that the ion of the gelling solution is a metal cation such as Ba^{2+} and other bivalent cations (col. 6, lines 39-42).

6. Claims 20 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmermann in view of Huang et al. as applied to claim 19 above, and further in view of Lim (US 4,352,883).

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Regarding claim 20, Zimmermann does not teach that the polyvalent cation of the gelling solution is selected from the group consisting of poly (allylamine hydrochloride), poly (ethylene imine), poly (diallyldimethylammonium chloride), polyamide-polyamine-epichlorhydrine, chitosan, amino-dextran, and protamine sulfate.

However, Lim teaches that the polyvalent cation of the gelling solution is polyethyleneimine (col. 7, lines 59-64).

It would have been obvious to one of ordinary skill in the art at the time of the invention to select polyethyleneimine as the polyvalent cation in the gelling solution in the method of Zimmermann since Lim teaches that polysaccharide can be (a) gelled to form a shape retaining mass by being exposed to a change in conditions such a pH change or by being exposed to multivalent cations such as Ca^{++} ; and (b) permanently “crosslinked” or hardened by polymers containing reactive groups such as amine or imine groups which can react with acidic polysaccharide constituents (col. 2, lines 37-46).

Regarding claim 28, Zimmermann teaches that the ion of the gelling solution is a metal cation such as Ba^{2+} and other bivalent cations.

Zimmermann does not positively teach that the metal cation of the gelling solution is Ca^{2+} .

However, Lim teaches that Ca^{2+} is used as the metal cation of the gelling solution (col. 2, lines 37-42).

It would have been obvious to one of ordinary skill in the art at the time of the invention to select Ca^{2+} as the metal cation of the gelling solution in the method of Zimmermann since Lim teaches that Ca^{2+} is a multivalent cation which forms crosslinked polymer microspheres with

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polysaccharide (col. 2, lines 37-42). The Ca cation is viewed as functional equivalent, providing gel.

7. Claims 29-30, 32 and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmermann in view of Huang et al. as applied to claim 18 above, and further in view of Andersson et al. (WO 03/091315).

Regarding claims 29-30 and 36, Zimmermann does not teach that the gelling solution additionally comprises a surfactant present in an amount of from 0.05 to .15% by weight.

However, Andersson et al. teach that droplets which form polysaccharide beads are collected in a bath comprised of a liquid having a reduced surface tension by adding a surfactant to the liquid (page 7, line25- page 8, line 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate the teaching of Andersson et al. in the method of Zimmermann to provide a surfactant in the gelling solution to facilitate movement of the beads in the solution.

Andersson et al. do not positively teach the amount of surfactant that is added, however, it would have been obvious to one of ordinary skill in the art to select an appropriate amount of surfactant to satisfactorily lower the surface tension of the solution. Additionally the amount of surfactant is known to affect particle size of the capsules.

Regarding claim 32 and 37, Zimmerman does not positively teach that the temperature of the solution of the ionically crosslinkable polyionic polymer according to step (a) is kept within a temperature of from 25 to 35 deg C. However, Andersson et al. teach the temperature of the polysaccharide solution should be kept low, such as below about 40 deg C (page 5, lines 2-4). It

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would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate the teaching of Andersson et al. in the method of Zimmermann since Andersson et al. teach that keeping the solution at a low temperature avoids formation of lumps (page 5, lines 2-4).

Regarding claim 35, Zimmerman does not teach filtering the microspheres through a screen.

However, Andersson et al. teach filtering the beads to a sieve 14 for particle concentration (page 13, line 5 and fig. 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to provide the filtering step as taught by Andersson et al. in the method of Zimmermann in order to obtain microspheres with a more uniform size distribution.

8. Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmerman in view of Huang et al. and Andersson et al. as applied to claim 29 above, and further in view of Lemoine et al. NPL document Preparation and characterization of alginate microspheres containing a model antigen).

Regarding claim 31, Andersson et al. do not positively teach that the surfactant is selected from the group consisting of polyoxyethylene sorbitans and surfactants comprising a block copolymer of ethylene oxide and/or propylene oxide.

However, Lemoine et al. teach the use of polyoxyethylene sorbitan trioleate as surfactant in the production of alginate microspheres (see section 2.1).

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It would have been obvious to one of ordinary skill in the art at the time of the invention to use polyoxyethylene sorbitan trioleate as surfactant in the method of Zimmermann since Lemoine et al. teach that polyoxyethylene sorbitan trioleate, or Tween 85 produced less heterogeneous and smaller microspheres (table 1 and section 3.1). Surfactant of Lemoine is viewed as functional equivalent.

9. Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmermann in view of Huang et al. as applied to claim 21 above, and further in view of Vasington et al. (US 5,387,522), Andersson et al. (WO 03/091315) and Lemoine et al. NPL document Preparation and characterization of alginate microspheres containing a model antigen).

Regarding claim 33, Zimmermann teaches that in step (a), the solution comprises about 2 % by weight sodium alginate (col. 2, lines 56-63). Zimmermann does not teach that the solution comprises of from 0.75% to 1.5% by weight of sodium alginate. Zimmermann does not positively teach that the sodium alginate is low viscosity.

However, Vasington et al. teach low viscosity sodium alginates that are used as the polyanionic polymer. Further, Vasington et al. teach that the concentration of the sodium alginates in the mixture should range from about 0.5 to about 1.4%, preferably about 0.6 to 1.2%, most preferably about 0.7-0.9% (col. 5, lines 17-51).

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate the teaching of Vasington et al. in the method of Zimmerman et al. since Vasington et al. teach that low percentage of sodium alginate result in higher porosity of the gel beads to nutrients and other factors (col. 5, line 46-51). Moreover, lowering the viscosity of

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sodium alginates produces smaller microspheres. Zimmermann teaches that the ion of the gelling solution is a metal cation such as Ba^{2+} and other bivalent cations. Zimmermann does not positively teach that the metal cation of the gelling solution is Ca^{2+} . However, Vasington et al. teach that the cation in the gelling solution is Ca^{2+} (col. 6, lines 46-48, col. 7, lines 28-32 and col. 8, lines 42-47).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use Ca^{2+} as the cation in the gelling solution as taught by Vasington et al. since Vasington et al. teach that Ca^{2+} forms stable calcium alginate gel containing entrapped cells (col. 8, lines 42-47).

Zimmermann does not teach that the gelling solution additionally comprises a surfactant present in an amount of from 0.05 to .15% by weight.

However, Andersson et al. teach that droplets which form polysaccharide beads are collected in a bath comprised of a liquid having a reduced surface tension by adding a surfactant to the liquid (page 7, line 25- page 8, line 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate the teaching of Andersson et al. in the method of Zimmermann to provide a surfactant in the gelling solution to facilitate movement of the beads in the solution.

Andersson et al. do not positively teach the amount of surfactant that is added, however, it would have been obvious to one of ordinary skill in the art to select an appropriate amount of surfactant to satisfactorily lower the surface tension of the solution. Andersson et al. do not positively teach that the surfactant is poly (oxyethylene) 20-sorbitane monolaurate.

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However, Lemoine et al. teach the use of polyoxyethylene sorbitan trioleate as surfactant in the production of alginate microspheres (see section 2.1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use polyoxyethylene sorbitan trioleate as surfactant in the method of Zimmermann since Lemoine et al. teach that polyoxyethylene sorbitan trioleate, or Tween 85 produced less heterogeneous and smaller microspheres (table 1 and section 3.1).

While Andersson et al. teach the use of polyoxyethylene sorbitan trioleate, as opposed to poly (oxyethylene) 20-sorbitane monolaureate as recited in claim 33.

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute polyoxyethylene sorbitan trioleate with poly (oxyethylene) 20-sorbitane monolaureate since both surfactants are structurally similar.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to XUE LIU whose telephone number is (571)270-5522. The examiner can normally be reached on Monday to Friday 9:30 - 6:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Katarzyna Wyrozebski can be reached on (571)272-1127. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/X. L./

Examiner, Art Unit 1791

/KAT WYROZEBSKI/

Supervisory Patent Examiner, Art Unit 1791